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DEPARTMENT OF THE AIR FORCE
HEADQUARTERS 27TH COMBAT SUPPORT GROUP (TAC)
CANNON AIR FORCE BASE, NM 88103

SEP 10 1991

04 SEP 1991

Mr. Benito Garcia, Chief
Hazardous & Radioactive Waste Bureau
New Mexico Environment Department
1190 St. Francis Drive
Santa Fe, New Mexico 87502

Re: Modification of Cannon AFB's Part B Operating Permit (NM7572124454)

Dear Mr. Garcia

Cannon AFB is requesting a Class II Modification to our DRMO storage facility's Part B Operating Permit. The requested changes are outlined in an attachment. As required by NMHWR-6, 270.42 we have sent a notice of the modification request to all persons on our mailing list and we are publishing the notice in the Clovis News Journal and the Portales News-Tribune. (A copy of the notice is attached for your review.) The request will be discussed during a public meeting on 24 Sep 91 at 1900 in the Town Hall of Clovis Community College.

Cannon AFB submitted a similar request on 15 Aug 90. However, based on your letter dated 30 Oct 90 and followup discussions with NMED representatives we determined that it would be better to wait until the NMED adopted the 1 Jul 90 edition of 40 CFR. The modification has been updated and several of the NMED's concerns (which were expressed in a letter dated 30 Oct 90) have been addressed in the requested modification. The other items of concern are discussed below.

1. Item 4. This item involved the justification for listing warfarin and phenol as "U" rather than "P" wastes. In order to determine the waste codes we referenced a "Waste Disposal Instructions" guidebook published by the United States Army Environmental Hygiene Agency (portions of which are attached). This guidebook, which lists the waste codes for hazardous materials in the Federal Supply System, listed the warfarin and phenol as "U" wastes. The base hospital does not generate these wastes on a regular basis and the DRMO will research and verify the waste code for each turn-in.

2. Item 10. A concern was raised over removing cartridge respiratory from the DRMO emergency equipment list. DRMO personnel are trained in hazardous material safety, health and fire prevention procedures as part of the Defense Hazardous Property Management Course. DRMS regulations,

however, do not allow DRMO personnel to respond to a spill. In the event of a spill they will immediately call the Fire Department. The Fire Department is located less than 1 mile from the storage facility. In the event of a release of hazardous material or waste anywhere on the base the Cannon AFB Fire Department will be the first responder. Fire Department personnel have received extensive spill response training and they maintain a HazMat response van which contains over $75,000 worth of spill response equipment. The Fire Department is prepared to provide on-scene command and control, on-site rescue and fire extinguishment. They will also stabilize the spill material by providing containment and countermeasures.

Any questions concerning this request may be directed to Mr. Jim Richards at (505) 784-4639.

Sincerely

David E. Benson

DAVID E. BENSON, Colonel, USAF
Commander

3 Atchs
1. Proposed Modification
2. Public Notice
3. Guidebook Excerpts

cc: Facility Mailing List w/o Atch 2 & 3
Mr. Bill Gallagher, EPA Region VI, w/o Atch 2 & 3
HQTAC/DEV w/o Atch 2 & 3

REQUESTED MODIFICATION TO CANNON AFB'S OPERATING PERMIT

1. Module III.B.1. The list of wastes which may be stored in the facility needs to be expanded to include:

Characteristic for Reactivity	D003	1,0001bs.	
Lead Wastes	D008	1,3001bs. 115 gals.	3 55-gal. drums
Mercury Wastes	D009	250 1bs.	
Lindane Wastes	D013	10 gals.	
Methyl Ethyl Ketone Wastes	D035	1,3001bs. 115 gals.	3 55-gal. drums
Discarded Chlorophenol formulations	F027	1,0001bs.	
Epinephrine	P042	10 gals.	
Formaldehyde	U122	10 gals.	
Phenol	U188	10 gals.	
Warfarin	U248	10 gals.	

These wastes are being added for a variety of reasons. Although they are not generated on a regular basis, materials such as lithium batteries (D003), mercury batteries (D009) and pentachlorophenol pallets (F027) may require disposal as a hazardous waste. Lead wastes need to be included in the permit for the reasons outlined in the NOV response dated 28 Jun 90. The third group of wastes that are being added are generated by the hospital. Small amounts (less than 1 gallon per year) lindane, formaldehyde, and phenol may need to be disposed of as hazardous waste either because their shelf life expired or after being used in a medical procedure.

2. Module III.B.2. The above wastes will be segregated as indicated below.

Ignitable Waste	Acute Hazardous Waste	Toxic Waste		Reactive Waste
D035	F027	D008	U188	D003
U122	P042	D009	U248	
		D013		

3. Permit Attachment A-1. The following changes should be made to the Waste Analysis Plan.

a. C-4. These statements about the generation of hazardous waste should be added as listed below.

"The Aerospace Ground Equipment branch, the Wheel and Tire shop, the Metals Technology shop and the Propulsion shop each have a bead blaster whose dust is characteristically hazardous due to metals such as lead, cadmium, and chromium. Wastes are collected at a satellite accumulation point in the respective shops for later transfer to DRMO."

"The Auto Hobby shop and the Civil Engineering paint shop generate small quantities (5-10 gallons per year) of paint related waste in the course of routine operations. Wastes are collected at a satellite accumulation point in the respective shops for later transfer to DRMO."

"The base hospital generates small quantities (less than 1 gallon per year) of phenol, lindane, and formaldehyde in the course of routine operations. On occasion outdated or off specification phenol, warfarin, epinephrine and formaldehyde must also be turned in as hazardous waste. All wastes are collected at satellite accumulation points in the hospital for later transfer to DRMO."

b. C-5. Three minor changes need to be made to reflect current base operations.

(1). Para 1. In the first sentence delete "and wipe down material."

(2). Para 1. Delete second sentence.

(3). Para 2. In the second sentence delete "B & B 3100."

c. C-5a-d. The waste analysis sheets have been updated to reflect the current waste generation streams. The sheet for B&B 3100 has been deleted and a sheet for bead blaster residue has been inserted.

d. C-10. In order to satisfy the requirements of 40 CFR 268, Land Disposal Restrictions, the following paragraph needs to be added to the end of the page. (In an NOV response dated 23 Sep 88, a similar paragraph was inserted on this page to meet the requirements of the "first third" ruling. This inclusion, however, was inadvertently left out of the final permit).

"In accordance with 40 CFR 268, Land Disposal Restrictions, Cannon will notify the receiving facility of all restricted and prohibited wastes requiring treatment prior to land disposal with the following reference, 'These wastes should be treated to the standards set by 40 CFR 268 Subpart D as applicable.' Additionally, a Restricted Waste Notification form as shown in Figure C-1a will accompany all restricted wastes. Test results or knowledge of process may be used to determine if the waste is restricted from land disposal."

e. In order to allow Cannon to have samples analyzed at a lab other than the USAF Occupational and Environmental Laboratory (OEHL) the following changes need to be made to the permit.

(1) C-14, Para 2. (a). At the end of the first sentence add: "or another lab which employs current SW-846 methods and can obtain the detection limits specified by that document."

(2) C-19 Para C.2.g. In the first sentence change "USAF OEHL" to "lab." In the third sentence change "OEHL" to "Lab."

f. References to EP Toxicity Method need to be replaced by Toxicity Characteristic Leaching Procedure (TCLP) in order to comply with the changes to NMHWR-6 261.

(1) C-16. Para 1. Change "EP Toxicity" to "TCLP."

(2) C-17. Figure C-3. Change "EP Tox." to "TCLP."

4. Permit Attachment A-2. The following items concern the "Test Methods for Evaluating Solid Waste" table.

a. Change "Extraction Procedure (EP) Toxicity Method" to "Toxicity Characteristic Leaching Procedure (TCLP)."

b. There will not be any new waste codes added to this table because it already included some of the new waste codes (D008 and D009). The waste codes not listed in this table (D003, D013, D035 and F027) will be identified based on user's knowledge of the product.

5. Permit Attachment E-2. D-13a. The new wastes identified in this modification need to be inserted in the "Description of Containers To Be Used to Store Hazardous Wastes at DRMO-Cannon."

a. The following materials should be added to the "Potassium dichromate, DDT" listing: "Formaldehyde, Epinephrine, Lindane and Warfarin."

b. Add the following to the table:

"Phenol Various 173.349 IAW 49 CFR 173.349"

6. Permit Attachment F. There are two minor changes which need to be made to the Contingency Plan.

a. G-29. Para 3. In the second sentence change "twenty thirty gallon drums" to "twenty eighty-five gallon drums."

b. G-33. Table G-4. Delete requirement for "MSA Ultra Twin Respirator and cartridges" from equipment list. DRMO personnel are not authorized hazard pay, and therefore, cannot use this equipment. Cannon's Fire Department, however, does maintain Self Contained Breathing Apparatus suits on its Spill Response Van.

The above changes, except for ones in the modules, have been incorporated into the text of the permit. Copies of the affected pages have been included as attachments to this proposed modification (pages C-4, C-5, C-5a-d, C-10, C-14, C-16, C-17, C-19, A-2, D-13a, G-29 and G-33).

PUBLIC NOTICE
MODIFICATION OF ENVIRONMENTAL PERMIT

Cannon AFB, NM is requesting comments on a proposal to modify the Resource Conservation and Recovery Act (RCRA) permit for the Defense Reutilization and Marketing Office (DRMO) hazardous waste storage facility. The proposed modification will update the permit to include additional industrial wastes and to describe new waste processes which are typically generated by aircraft maintenance activities. The comment period begins with the publishing of this notice and will continue for 60 days.

A public hearing will be held on 25 Sep 91 at 1900 in the Town Hall of the Clovis Community College. Copies of the modification request can be viewed and copied at Cannon AFB's Environmental Management Office (Bldg. 250). Contact Mr. Jim Richards at 784-4639 for more information regarding the request or the meeting . Written comments concerning the modification may be sent to the agency contact person: Mr. Edward Horst, Hazardous and Radioactive Materials Bureau, New Mexico Environment Department, 1190 St. Francis Dr., P.O. Box 26110, Santa Fe, NM 87502.

The permittee's compliance history during the life of the permit being modified is available from the agency contact person.

TG 126

UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010-5422

A E H A

WASTE DISPOSAL INSTRUCTIONS

This copy is a reprint which includes current pages from Changes 1 through 6.

CONTENTS

CHAPTER 1
Introduction

1-1. Purpose

This guide is designed to provide methods of disposal for small quantities of unserviceable/uncontaminated materiel identified in the Federal Supply System. The specific listed items are based on identified user needs and do not purport to include the universe of materiel that may require disposal. The guide is written primarily for Department of the Army users, but is applicable to all Department of Defense activities.

1-2. References

Required and related publications are listed in Appendix A.

1-3. Explanation of Terms

To better understand the requirements set out in this guide, the definitions of should and shall follow:

a. Shall: Indicates a requirement that is necessary or essential to meet the currently accepted standards of protection or Federal rules and regulations.

b. Should: Indicates an advisory recommendation that is to be applied when practicable.

1-4. Suggested Improvements

The proponent of this guide is the US Army Environmental Hygiene Agency. Users are invited to send comments and suggested improvements on DA Form 2028 (Recommended Changes to Publications and Blank Forms) directly to Commander, US Army Environmental Hygiene Agency, ATTN: HSHB-ME-SH, Aberdeen Proving Ground, MD 21010-5422.

1-5. Technical Assistance

Technical assistance and guidance on proper disposal of unservicable/ uncontaminated materiel can be obtained from Commander, US Army Environmental Hygiene Agency, Waste Disposal Engineering Division, Aberdeen Proving Ground, MD 21010-5422, AUTOVON 584-3651.

Chapter 2
General

2-1. Coordination

Coordination shall be established with the installation environmental coordinator prior to beginning any disposal operations. The environmental coordinator will:

a. Know if your installation is a small or large quantity generator.

b. Know if permits are required for the disposal operation.

c. Coordinate with Federal, State and local regulatory agencies, if necessary.

2-2. Hazardous Waste Training

a. Hazardous Waste Generator. If you are a hazardous waste generator and are storing for less than 90 days and are not exempt under the provisions of satellite storage (40 CFR 262.34, Accumulation Time), facility personnel must successfully complete a program of classroom instruction or on-the-job training that teaches them to perform their duties in a way that ensures the facility's compliance with the requirements of 40 CFR 265. Specific training requirements appear in 40 CFR 265.16 (Personnel Training).

b. Owners and Operators of Hazardous Waste Treatment, Storage, and Disposal Facilities. If you are an owner or operator of a hazardous waste treatment, storage and disposal facility, facility personnel must successfully complete a program of classroom instruction or on-the-job training that teaches them to perform their duties in a way that ensures the facility's compliance with the requirements of 40 CFR 264. Specific training requirements appear in 40 CFR 264.16 (Personnel Training).

2-3. Hazardous Waste Technical Assistance

Additional assistance and guidance contacts are shown in Appendix B.

2-4. Management Information

a. The methods of disposal identified have been developed based on the Federal laws of the United States and are intended to provide state-of-the-art technical guidance for disposal operations. Local and State laws, as well as the environmental laws of foreign governments, may be more stringent than the provisions contained in this guide. In such cases, disposal operations shall comply with the environmental requirements of the local, State, or foreign government. It is the responsibility of each activity to ensure that local, State, and foreign laws are not violated prior to using any disposal instruction shown in this guide.

b. Requests for methods of disposal for materiel that do not appear in this guide should be addressed to Commander, US Army Environmental Hygiene Agency, ATTN: HSHB-ME-SH, Aberdeen Proving Ground, MD 21010-5422 (AUTOVON 584-3651). The following information is required to develop a method of disposal:

(1) National Stock Number (NSN) or locally assigned stock number. [In order to develop a disposal instruction for a locally assigned stock number, the information in (2) - (7) must be provided.]

(2) Name (proper and/or trade)

(3) Quantity for disposal

(4) Chemical Abstract Service (CAS) number, if known

(5) Condition of disposal item and its container

(6) Manufacturer (include address and telephone number, if available)

(7) Ingredients and their percentages

(8) Installation point of contact, mailing address, and AUTOVON number

(9) Urgency of request (priority or routine)

c. Nonhalogenated, nonchlorinated solvents exhibiting a hazardous waste characteristic (40 CFR 261, Subpart C) may be considered for waste fuel blending (40 CFR 266, Subparts D and E). Before any blending of these solvents is attempted, coordination must be obtained from the applicable installation hazardous waste manager, MACOM, and State regulatory authority. All applicable Federal, State and local regulations will be met. Assistance on waste fuel blending can be obtained from USAEHA, Waste Disposal Engineering Division, AUTOVON 584-3651.

2-5. Basis and Limitations

a. These disposal instructions were developed for use:

(1) By or under the supervision of personnel familiar with chemicals and their dangers if mishandled.

(2) By personnel concerned with the protection of health and the environment.

Generally, disposal personnel will not need special skills and training; but if such are needed, the instruction will so state.

b. The instructions reflect the best judgments of health and environmental experts at this Agency and the best known state-of-the-art at the time they are issued. They are primarily based upon published reference books, special studies, field experience, or recognized experts. Consideration is given to chemical, physical and toxicological properties, packaging, quantity and container conditions. These instructions incorporate all current requirements, standards, and guidelines issued by Federal agencies. Applicable State and local laws and regulations may not be reflected, but shall be determined and followed.

c. All disposal facilities shall be permitted, and disposal shall be in compliance with this permit. If possible, alternative disposal methods are given. When necessary, safety precautions are given to protect the health of disposal personnel and other persons nearby.

2-6. Approved Methods of Disposal.

a. An explanation of terms is contained in Appendix C, Section I. Table C-1 shows the Federal Supply Classes which are included in this technical guide. Section II contains the approved methods of disposal in NSN order. Section III contains the approved methods of disposal in nomenclature order. Specific information is provided for a hazardous waste NSN.

b. Standardized disposal paragraphs are addressed in Appendix D, Section I. Table D-1 explains the disposal instruction identifiers. Disposal instruction narratives in alphabetic/numeric order are provided in Section II.

SECTION III. APPROVED METHODS OF DISPOSAL BY NOMENCLATURE

NOMENCLATURE	NSN	RC	IN	SLF	SS	CC	SP	EPA HAZ WASTE NO.	EPA HAZ CODES	DISP CODE
Pentachlorophenol Lumber	6810-00-SWM-0126					X		F027	H	HW01
Pentane Tech	6810-00-070-0891					X		D001	I	HW01
Pentane Tech	6810-00-973-9746					X		D001	I	HW01
Pentane Tech	6810-00-984-9784					X		D001	I	HW01
Pentrating Oil 1gal	9150-00-223-4119	X								RM03
Perchloric Acid 60% ACS Liq	6810-00-275-8129					X		D002	CR	HW01
Perchloric Acid 70%	6810-00-753-4792					X		D002	CR	HW01
Perchloric Acid 70% 500ml	6810-01-119-7675					X		D002	CR	HW01
Perchloroethylene Solvent	6810-00-MIS-0426					X		U210	T	HW01
Periodic Acid	6810-00-MIS-0716					X		D002	C	HW15
Permount	6810-00-MIS-0498		X							A001
Petroleum Ether	6810-00-584-3079						X	D001	I	RM11
Petroleum Ether Liq 1gal	6810-00-051-5872						X	D001	I	RM11
Petroleum Ether Liq 5gal	6810-00-227-1307						X	D001	I	RM11
Phenazopyridine Hcl Tab	6505-00-582-5344					X			T	HWA2
Phenazopyridine Hcl Tab	6505-00-C99-4133					X			T	HWA2
Phenazopyridine Hcl Tab 0.1g 100	6505-00-138-8461					X			T	HWA2
Phenazopyridine Hcl Tab 0.1g 50	6505-00-582-5346					X			T	HWA2
Phenazopyridine Hcl Tab 100mg IS100	6505-01-153-3253					X			T	HWA2
Phenelzine Dihydrogen	6810-00-MIS-0702					X		D001	I	HW01
Phenidone	6810-00-MIS-0476			X	X					CB01
Phenol	6505-00-234-2009					X		U188	T	HW01
Phenol	6810-00-023-0836					X		U188	T	HW01
Phenol	6810-00-569-1191					X		U188	T	HW01
Phenol	6810-00-754-0325					X		U188	T	HW01
Phenol	6810-00-973-6490					X		U188	T	HW01
Phenol 1#	6505-00-133-9920					X		U188	T	HW01
Phenol 4oz	6810-00-234-2009					X		U188	T	HW01
Phenol USP (Carbolic Acid)	6505-00-133-9905					X		U188	T	HW01
Phenolphthalein ACS	6810-00-134-0000		X	X						AC01
Phenolphthalein Brine	6810-00-374-3043		X	X						AC01
Phenolphthalein Pwdr 4oz	6810-00-223-7612		X	X						AC01
Phenolphthalein Sol 1/2oz	6810-00-798-9643		X	X						AC01
Phenolphthalein Sol 16oz	6810-00-282-2909		X	X						AC01
Phenolphthalein Sol 1oz	6810-00-445-0449		X	X						AC01
Phenolphthalein Sol 2oz	6810-00-227-1857		X	X						AC01
Phenyl Salicylate	6810-00-MIS-0724		X	X						AC01
Phenyl-p-Quinine	6810-00-MIS-0567					X		D001	I	HW01
Phenylhydrazine Hcl	6810-00-MIS-0589					X			T	HW01
Phenylmercuric Acetate Antisep Jell	6505-00-C99-4398					X		P092	H	HW01
Phenytoin	6630-01-143-2445					X			T	HWA2
Phenytoin Inj 100mg 2ml	6505-01-211-9769					X			T	HWA2
Phenytoin Oral Susp	6505-00-890-1110					X			T	HWA2
Phenytoin Oral Susp	6505-00-C99-4619					X			T	HWA2
Phenytoin Oral Susp 5ml 100	6505-01-111-2108					X			T	HWA2

SECTION III. APPROVED METHODS OF DISPOSAL BY NOMENCLATURE

NOMENCLATURE	NSN	RC	IN	SLF	SS	CC	SP	EPA HAZ WASTE NO.	EPA HAZ CODES	DISP CODE
Vitadye	6505-00-MIS-0208					X		D001	I	HW01
Warfarin Sodium Salt 2.5mg 100	6505-00-C99-2939					X		U248	T	HW01
Warfarin Sodium Salt 2mg 100	6505-00-982-4230					X		U248	T	HW01
Warfarin Sodium Salt 5mg 100	6505-00-982-4229					X		U248	T	HW01
Warfarin Sodium Salt Tab 10mg	6505-00-C99-4276					X		U248	T	HW01
Warfarin Sodium Salt Tab 10mg	6505-00-C99-4498					X		U248	T	HW01
Warfarin Sodium Salt Tab 10mg 100	6505-00-482-2725					X		U248	T	HW01
Warfarin Sodium Salt Tab 2.5mg	6505-00-C99-5368					X		U248	T	HW01
Warfarin Sodium Salt Tab 2.5mg 100	6505-00-728-2616					X		U248	T	HW01
Warfarin Sodium Salt Tab 2mg 200	6505-00-148-9735					X		U248	T	HW01
Warfarin Sodium Salt Tab 5mg 100	6505-00-149-0317					X		U248	T	HW01
Warfarin Sodium Tab	6505-00-C99-6166					X		U248	T	HW01
Waste Petroleum Products (POL)	6800-00-SWM-0004	X								RM03
Water Distilled 1gal	6810-00-682-6867				X					B005
Water Distilled 5gal	6810-00-356-4936				X					B005
Water Distilled ACS	6810-00-107-1510				X					B005
Water Distilled Tech 14.4 fl oz	6810-00-584-3161				X					B005
Water Purification Tab Iodine	6850-00-985-7166			X						C100
Water Softener	7930-00-C90-0242			X	X					CB01
Wetting Agent	6850-00-135-4700			X	X					CB01
Wetting Agent	6850-00-143-2100			X	X					CB01
Wetting Agent	6850-00-889-7494			X	X					CB01
Wetting Agent Liquid 30ml	6850-01-169-0293			X	X					CB01
Whipcide Tab 2 912mg 100	6840-00-MIS-0038			X						C107
Whipcide Tab 3 2.28gr 25	6840-00-MIS-0039			X						C107
Whipcide Tab 456mg 100	6840-00-MIS-0037			X						C107
Wire Nonelectrical	9545-00-448-9010	X								RM02
Wire Nonelectrical	9545-99-448-9110	X								RM02
Wire Nonelectrical Silver 1oz	9545-00-127-7124	X								RM02
Wood Preservative (Penta)	8030-00-MIS-0003					X		F027	H	HW01
Wood Preservative Penta Grease	8030-00-MIS-0002					X		F027	H	HW01
Wood Preservative Penta Mixture1gal	8030-00-282-0970					X		F027	H	HW01
Wood Preservative Tetra/Chloro/Pent	8030-00-616-3970					X		F027	H	HW01
Wright Blood Stain Tab wMethyl Alco	6505-00-149-6010					X		D001	I	HW01
Xanthydrol	6810-00-MIS-0734		X	X						AC01
Xylene	6810-00-068-8867						X	U239	I	RM11
Xylene	6810-00-072-2924						X	U239	I	RM11
Xylene	6810-00-086-3627						X	U239	I	RM11
Xylene	6810-00-099-3400						X	U239	I	RM11
Xylene	6810-00-149-7005						X	U239	I	RM11
Xylene	6810-00-201-0989						X	U239	I	RM11
Xylene	6810-00-227-1253						X	U239	I	RM11
Xylene	6810-00-281-1866						X	U239	I	RM11
Xylene	6810-00-290-4165						X	U239	I	RM11
Xylene	6810-00-300-6330						X	U239	I	RM11

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COUMADIN®

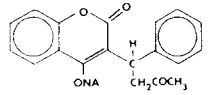
[ku'ma-din]

(Crystalline Warfarin Sodium, U.S.P.)

TABLETS

DESCRIPTION

COUMADIN® (crystalline warfarin sodium), a vitamin K dependent factor anticoagulant, is chemically crystalline sodium warfarin isopropanol clathrate. The crystalline form of warfarin sodium virtually eliminates trace impurities present in amorphous warfarin sodium, thus achieving a crystalline product of the highest purity. Warfarin is a coined generic name for 3-(α-Acetonylbenzyl)-4-hydroxycoumarin. Its empirical formula is $C_{19}H_{15}NaO_4$ and its structural formula may be represented by the following:



Warfarin sodium crystalline occurs as a white, odorless, crystalline powder, is discolored by light and is very soluble in water; freely soluble in alcohol; very slightly soluble in chloroform and in ether.

COUMADIN Tablets for oral use also contain:

All strengths:	Lactose, starch and other ingredients
2 mg	FD&C Blue 2 and FD&C Red 40
2½ mg	FD&C Blue 1 and D&C Yellow 10
5 mg	FD&C Red 3 and FD&C Yellow 6
7½ mg	D&C Yellow 10 and FD&C Yellow 6
10 mg	Dye Free

CLINICAL PHARMACOLOGY

COUMADIN and other coumarin anticoagulants act by inhibiting the synthesis of vitamin K dependent coagulation factors. The resultant **in vivo** effect is a sequential depression of Factors VII, IX, X and II. The degree of depression is dependent upon the dosage administered. Anticoagulants have no direct effect on an established thrombus, nor do they reverse ischemic tissue damage. However, once a thrombus has occurred, anticoagulant treatment aims to prevent further extension of the formed clot and prevents secondary thromboembolic complications which may result in serious and possible fatal sequelae.

After oral administration, absorption is essentially complete, and maximal plasma concentrations are reached in 90 minutes to 9 hours. Approximately 97% is bound to albumin within the plasma. COUMADIN usually produces its anticoagulant effect in 36 to 72 hours, and its duration of action may persist for 4 to 5 days, thus producing a smooth, long lasting effect. By curve COUMADIN is metabolized by hepatic microsomal enzymes to inactive metabolites that are excreted in the urine. reabsorbed and excreted into the urine.

INDICATIONS AND USAGE

COUMADIN is indicated for the prophylaxis and/or treatment of venous thrombosis and its extension, pulmonary embolism, atrial fibrillation with embolization, and as an adjunct in the prophylaxis of systemic embolism after myocardial infarction.

CONTRAINDICATIONS

Anticoagulation is contraindicated in any localized or general physical condition or personal circumstance in which the hazard of hemorrhage might be greater than the potential clinical benefits of anticoagulation, such as:

Pregnancy—COUMADIN is contraindicated in women who are or may become pregnant because the drug crosses through the placental barrier and may cause fatal hemorrhage to the fetus in utero. Furthermore, there have been reports of birth malformations in children born to mothers who have been treated with warfarin during pregnancy. Women of childbearing potential who are candidates for anticoagulant therapy should be carefully evaluated and the indications critically reviewed with the patient. If the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the possibility of termination of the pregnancy should be discussed in light of those risks.

Hemorrhagic tendencies or blood dyscrasias.

Recent or contemplated surgery of: (1) central nervous system, (2) eye, (3) traumatic surgery resulting in large open surfaces.

Bleeding tendencies associated with active ulceration or overt bleeding of: (1) gastrointestinal, genitourinary, respiratory tracts; (2) cerebrovascular hemorrhage; (3) aneurysms-cerebral, dissecting aorta; (4) pericarditis and pericardial effusions; (5) bacterial endocarditis.

Threatened abortion, eclampsia and preeclampsia.

Inadequate laboratory facilities or unsupervised senility, alcoholism, psychosis; or lack of patient cooperation.

Spinal puncture and other diagnostic or therapeutic procedures with potential for uncontrollable bleeding.

Miscellaneous: major regional, lumbar block anesthesia or malignant hypertension.

WARNINGS

The most serious risks associated with anticoagulant therapy with sodium warfarin are hemorrhage in any tissue or organ and, less frequently, necrosis and/or gangrene of skin and other tissues. The risk of hemorrhage is related to the level of intensity and the duration of anticoagulant therapy. Hemorrhage and necrosis have in some cases been reported to result in death or permanent disability. Necrosis appears to be associated with local thrombosis and usually appears within a few days of the start of anticoagulant therapy. In rare cases of necrosis, treatment through debridement or amputation of the affected tissue, limb, breast or penis has been reported. Careful diagnosis is required to determine whether necrosis caused by an underlying disease. Warfarin therapy should be discontinued when warfarin is suspected to be the cause of developing necrosis and heparin therapy may be considered for anticoagulation. Although various treatments have been attempted, no treatment for necrosis has been considered uniformly effective. See below for information on predisposing conditions. These and other risks associated with anticoagulant therapy must be weighed against the risk of thrombosis or embolization in untreated cases.

COUMADIN is a potent drug with a half-life of 2½ days; therefore its effects may become more pronounced as daily maintenance doses overlap. It cannot be emphasized too strongly that treatment of each patient is a highly individualized matter. Dosage should be controlled by periodic determinations of prothrombin time or other suitable coagulation tests. Determinations of whole blood clotting and bleeding times are not effective measures for control of therapy. Heparin prolongs the one-stage prothrombin time. When heparin and COUMADIN are administered concomitantly, refer to CONVERSION FROM HEPARIN THERAPY for recommendations.

Caution should be observed when COUMADIN is administered in any situation or in the presence of any predisposing condition where added risk of hemorrhage or necrosis is present.

Anticoagulation therapy with COUMADIN may enhance the release of atheroma plaque emboli, which may cause the Purple Toe Syndrome. These atheroma emboli may produce ischemic complications. Discontinuing COUMADIN therapy is recommended. The condition has been reported to be reversible.

Administration of anticoagulants in the following conditions should be based upon clinical judgment in which the risks of anticoagulant therapy are weighed against the risk of thrombosis or embolization in untreated cases. The following may be associated with these increased risks:

Lactation—COUMADIN appears in the milk of nursing mothers in an inactive form. Infants nursed by COUMADIN treated mothers had no change in prothrombin times. Effects in premature infants have not been evaluated.

Severe to moderate hepatic or renal insufficiency.

Infectious diseases or disturbances of intestinal flora – prolonged antibiotic therapy.

Trauma which may result in internal bleeding.

Surgery or trauma resulting in large exposed raw surfaces.

Indwelling catheters.

Severe to moderate hypertension.

Known or suspected deficiency in protein C—This hereditary or acquired condition, which should be suspected if there is a history of recurrent episodes of thromboembolic disorders in the patient or in the family, has been associated with an increased risk of developing necrosis following warfarin administration. Tissue necrosis may occur in the absence of protein C deficiency. It has been reported that concomitant anticoagulation therapy with heparin for 5 to 7 days during initiation of therapy with COUMADIN may minimize the incidence of this reaction. Warfarin therapy should be discontinued when warfarin is suspected to be the cause of developing necrosis and heparin therapy may be considered for anticoagulation.

Miscellaneous: polycythemia vera, vasculitis, severe diabetes, severe allergic and anaphylactic disorders.

Patients with congestive heart failure may become more sensitive to COUMADIN, thereby requiring more frequent laboratory monitoring, and reduced doses of COUMADIN.

Concurrent use of anticoagulants with streptokinase or urokinase is not recommended and may be hazardous. Please see recommendations accompanying these preparations.

PRECAUTIONS

Periodic determination of prothrombin time or other suitable coagulation test is essential.

Numerous factors, alone or in combination, including travel, changes in diet, environment, physical state and medication may influence response of the patient to anticoagulants. It is generally good practice to monitor the patient's response with additional prothrombin time determinations in the period immediately after discharge from the hospital, and whenever other medications are initiated, discontinued or taken haphazardly. The following factors are listed for your reference; however, other factors may also affect the anticoagulant response.

The following factors, alone or in combination, may be responsible for INCREASED PT response.

ENDOGENOUS FACTORS:

cancer	hepatic disorders– infectious hepatitis jaundice
collagen disease	
congestive heart failure	hyperthyroidism
diarrhea	poor nutritional state
elevated temperature	steatorrhea
	vitamin K deficiency

EXOGENOUS FACTORS:

alcohol†	ibuprofen
allopurinol	indomethacin
aminosalicylic acid	influenza virus vaccine
amiodarone HCl	mefenamic acid
anabolic steroids	methyldopa
anesthetics, inhalation	methylphenidate
antibiotics	metronidazole
bromelains	miconazole
chloral hydrate†	monoamine oxidase inhibitors
chlorpropamide	nalidixic acid
chymotrypsin	naproxen
cimetidine	narcotics, prolonged
clofibrate	pentoxifylline
COUMADIN overdosage	phenylbutazone
dextran	phenytoin
dextrothyroxine	pyrazolones
diazoxide	quinidine
diflunisal	quinine
diuretics†	ranitidine†
disulfiram	salicylates
ethacrynic acid	sulfinpyrazone
fenoprofen	sulfonamides, long acting
glucagon	sulindac
hepatotoxic drugs	tamoxifen
	thyroid drugs
	tolbutamide
	trimethoprim/sulfamethoxazole

also: other medications affecting blood elements which may modify hemostasis
- dietary deficiencies
- prolonged hot weather
- unreliable prothrombin time determinations

†Increased and decreased prothrombin time responses have been reported.

The following factors, alone or in combination, may be responsible for DECREASED PT response:

ENDOGENOUS FACTORS:

edema	
hereditary coumarin resistance	
hyperlipemia	
hypothyroidism	

EXOGENOUS FACTORS:

adrenocortical steroids	ethchlorvynol
alcohol†	glutethimide
aminoglutethimide	griseofluvin
antacids	haloperidol
antihistamines	meprobamate
barbiturates	oral contraceptives
carbamazepine	paraldehyde
chloral hydrate†	primidone
chlordiazepoxide	ranitidine†
cholestyramine	rifampin
COUMADIN underdosage	trazadone
diuretics†	vitamin C

also: diet high in vitamin K
unreliable PT determinations

†Increased and decreased prothrombin time responses have been reported.

Because a patient may be exposed to a combination of the above factors, the net effect of COUMADIN on PT response may be unpredictable. More frequent PT monitoring is therefore advisable. Medications of unknown interaction with coumarins are best regarded with caution. When these medications are started or stopped, more frequent PT monitoring is advisable. Coumarins may also affect the action of other drugs. Hypoglycemic agents (chlorpropamide and tolbutamide) and anticonvulsants (phenytoin and phenobarbital) may accumulate in the body as a result of interference with either their metabolism or excretion.

Special Risk Patients: Caution should be observed when warfarin sodium is administered to certain patients such as the elderly or debilitated or when administered in any situation or physical condition where added risk of hemorrhage is present.

Information for Patients: The objective of anticoagulant therapy is to control the coagulation mechanism so that thrombosis is prevented, while avoiding spontaneous bleeding. Effective therapeutic levels with minimal complications are in part dependent upon cooperative and well-instructed patients who communicate effectively with their physician. Various COUMADIN patient educational guides are available to physicians on request. Patients should be advised: Strict adherence to prescribed dosage schedule is necessary. Do not take or discontinue any other medication, except on advice of physician. Avoid alcohol, salicylates (e.g. aspirin), large amounts of green leafy vegetables and/or drastic changes in dietary habits, which may affect COUMADIN therapy. COUMADIN may cause a red-orange discoloration of alkaline urine. The patient should notify the physician if any illness, such as diarrhea, infection or fever develops or if any unusual symptoms, such as pain, swelling or discomfort appear or if prolonged bleeding from cuts, increased menstrual flow or vaginal bleeding, nosebleeds or bleeding of gums from brushing, unusual bleeding or bruising, red or dark brown urine, red or tar black stools or diarrhea occurs.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity and mutagenicity studies have not been performed with COUMADIN. The reproductive effects of COUMADIN have not been evaluated.

Use in Pregnancy: Pregnancy Category X–"See CONTRAINDICATIONS."

Pediatric Use: Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS

Potential adverse reactions to COUMADIN (crystalline warfarin sodium) may include:

- Hemorrhage from any tissue or organ. This is a consequence of the anticoagulant effect. The signs and symptoms will vary according to the location and degree or extent of the bleeding. Hemorrhagic complications may present as paralysis; headache, chest, abdomen, joint or other pain; shortness of breath, difficult breathing or swallowing; unexplained swelling; or unexplained shock. Therefore, the possibility of hemorrhage should be considered in evaluating the condition of any anticoagulated patient with complaints which do not indicate an obvious diagnosis. Bleeding during anticoagulant therapy does not always correlate with prothrombin activity. (See OVERDOSAGE–Treatment.)

  Bleeding which occurs when the prothrombin time is within the therapeutic range warrants diagnostic investigation since it may unmask a previously unsuspected lesion, e.g. tumor, ulcer, etc.
- Necrosis of skin and other tissues. (See WARNINGS.)
- Other adverse reactions are infrequent and consist of alopecia, urticaria, dermatitis, fever, nausea, diarrhea, abdominal cramping, a syndrome called "purple toes", cholestatic hepatic injury, and hypersensitivity reactions.
- Priapism has been associated with anticoagulant administration, however, a causal relationship has not been established.

OVERDOSAGE

Signs and Symptoms: Suspected or overt abnormal bleeding (i.e., appearance of blood in stools or urine, hematuria, excessive menstrual bleeding, melena, petechiae, excessive bruising or persistent oozing from superficial injuries) are early manifestations of anticoagulation beyond a safe and satisfactory level.

Treatment: Excessive anticoagulation, with or without bleeding, may be controlled by discontinuing COUMADIN therapy and if necessary, by administration of oral or parenteral vitamin K_1. (Please see recommendations accompanying vitamin K_1 preparations prior to use.)

Such use of vitamin K_1 reduces response to subsequent COUMADIN therapy. Patients may return to a pretreatment thrombotic status following the rapid reversal of a prolonged PT. Resumption of COUMADIN administration reverses the effect of vitamin K, and a therapeutic PT can again be obtained by careful dosage adjustment. If rapid anticoagulation is indicated, heparin may be preferable for initial therapy.

If minor bleeding progresses to major bleeding, give 5 to 25 mg (rarely up to 50 mg) parenteral vitamin K_1. In emergency situations of severe hemorrhage, clotting factors can be returned to normal by administering 200 to 500 ml of fresh whole blood or fresh frozen plasma, or by giving commercial Factor IX complex. Purified Factor IX preparations should not be used because they cannot increase the levels of prothrombin, Factor VII and Factor X which are also depressed along with the levels of Factor IX as a result of COUMADIN treatment. Packed red blood cells may also be given if signifi-

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